

8 SHEETS ~~DRWS~~ DRWS

Figure 1

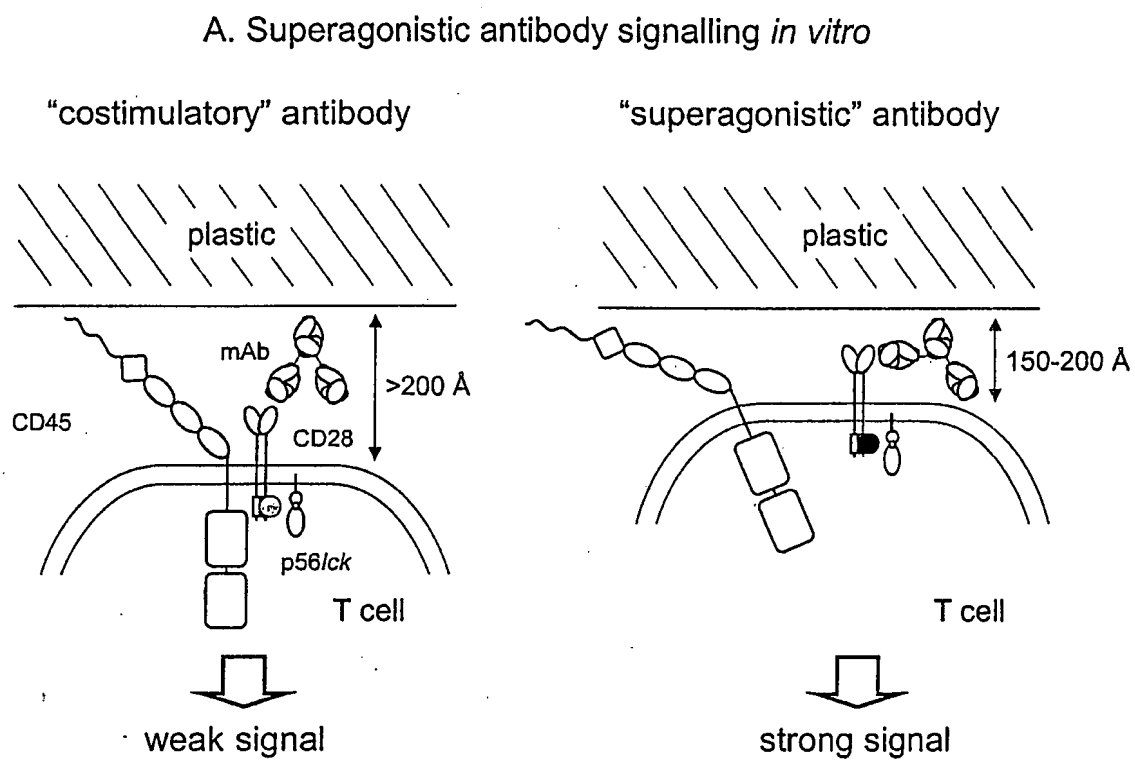


Figure 1

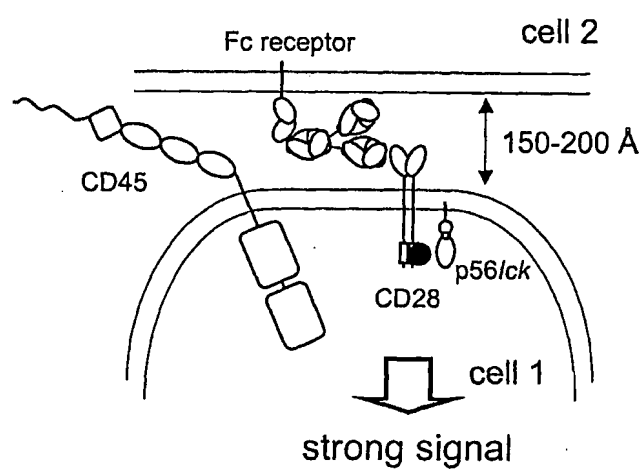
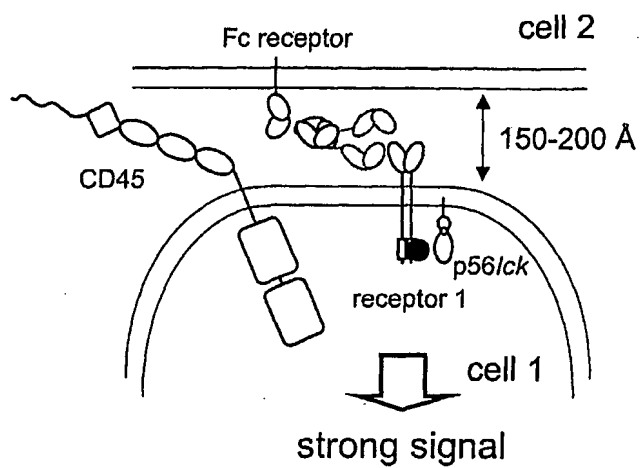
B. Superagonistic antibody signalling *in vivo*

Figure 1

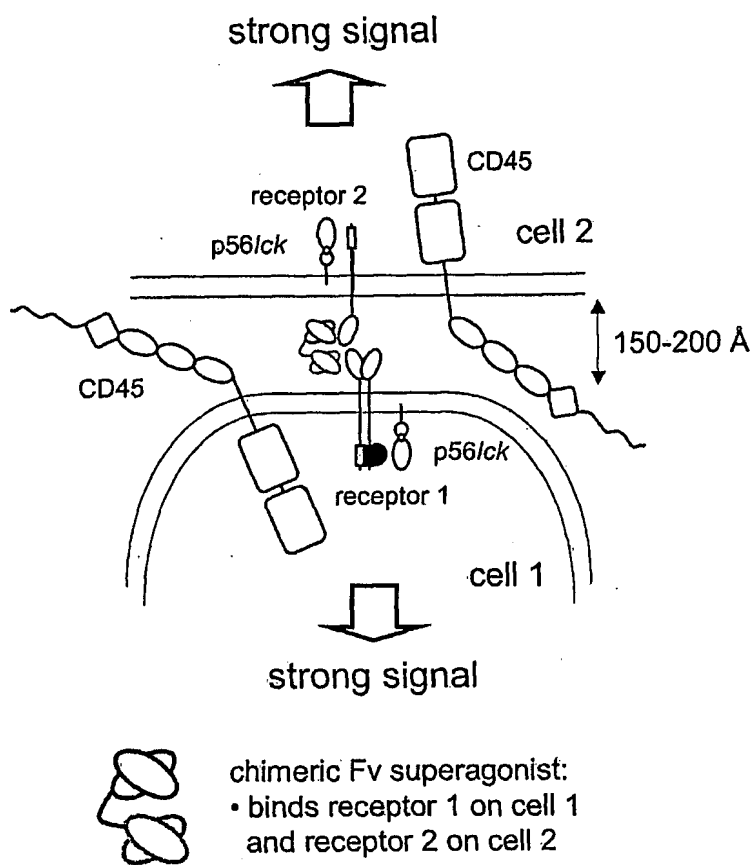
## C. Chimeric protein 1 (ligand-based)



chimeric ligand/Fc superagonist:  
• binds Fc receptor on cell 1  
and receptor 2 on cell 2

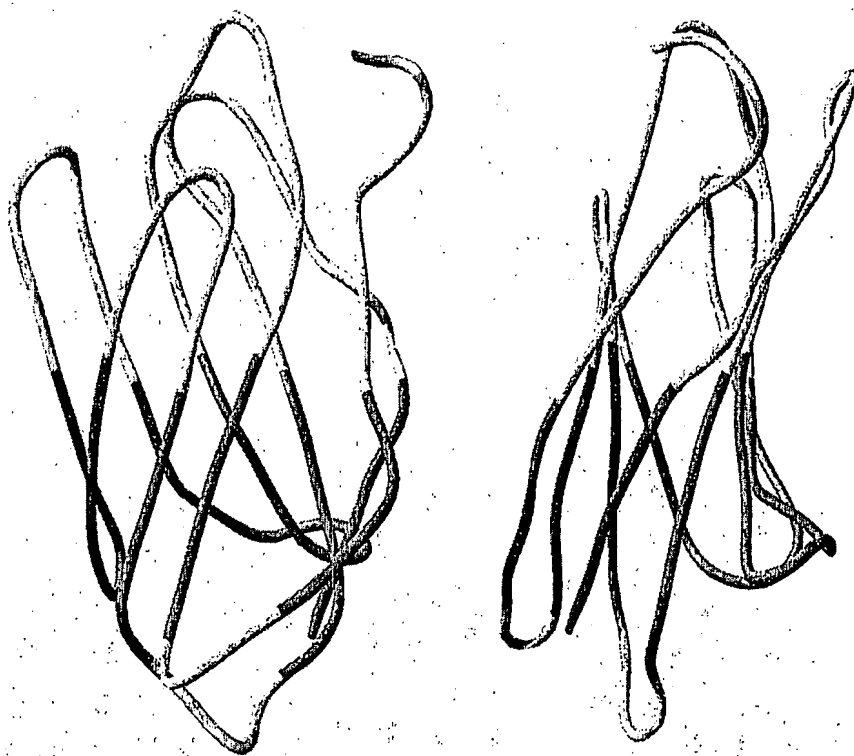
Figure 1

## D. Chimeric protein 2 (Fv-based)



A

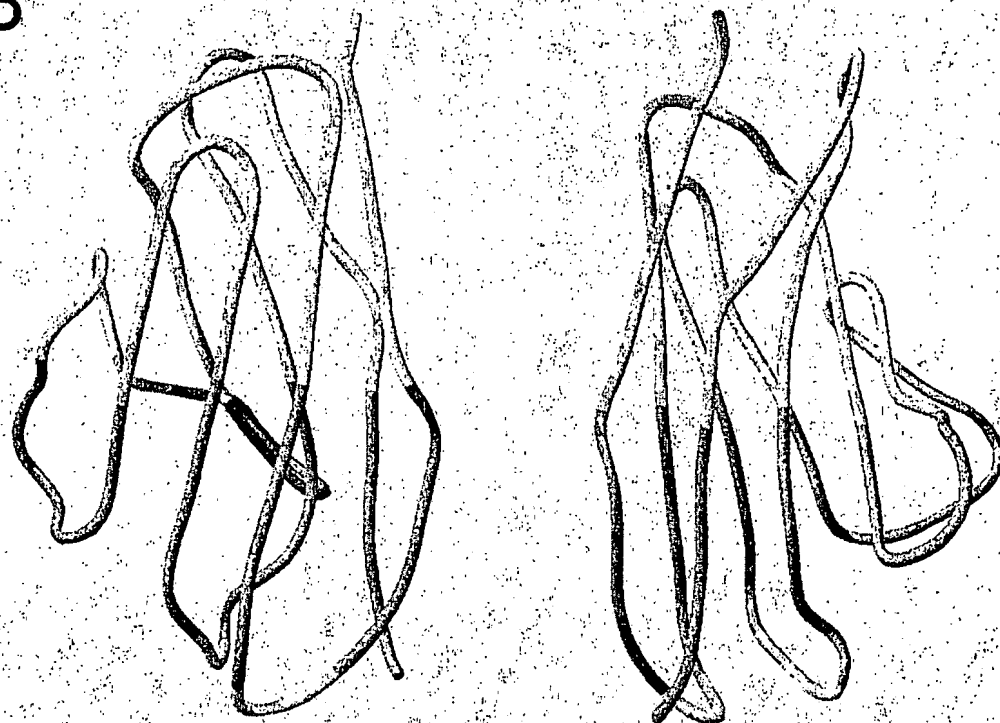
Figure 2



		A	A'	B	C	
hCD28	1	K I L V . K Q S P M L V A Y D N A V . N L S C K Y S Y N L E S R E F R A S L H K	38			
hCTLA-4	1	A M H V . A Q P A V V L A S S R G A S F V C E Y A S P G K A T E V R V I V L R	39			
hICOS	1	E I N G S A N Y E M F I F H N G G V . Q I L C K Y P D I V . Q Q F K M Q L L K	37			
					*	*
		C'	C''	D	E	
hCD28	39	G L D S A V . E V C V V Y G N Y S Q Q L Q V Y S K T G F N C D G K L G N E S V T	77			
hCTLA-4	40	Q A D S Q V T E V C A A T Y M M G N E L T F L D D S . I C T G T S S G N Q V N	77			
hICOS	38	G G . . Q I . . L C D L T K T K G S G N T V S I K S L K F C H S Q L S N N S V S	73			
			*	*	*	*
		E	F	G		
hCD28	78	F Y L Q N L Y V N Q T D I Y F C K I E V M Y P P P Y L D N E K S N G T I I H V	116			
hCTLA-4	78	L T I Q G L R A M D T G L Y I C K V E L M Y P P P Y L G . I G N G T Q I Y V	115			
hICOS	74	F F L Y N L D H S H A N Y Y F C N L S I F D P P P F K V T . . L T G G Y L H I	110			
			*	*	*	

Figure 2

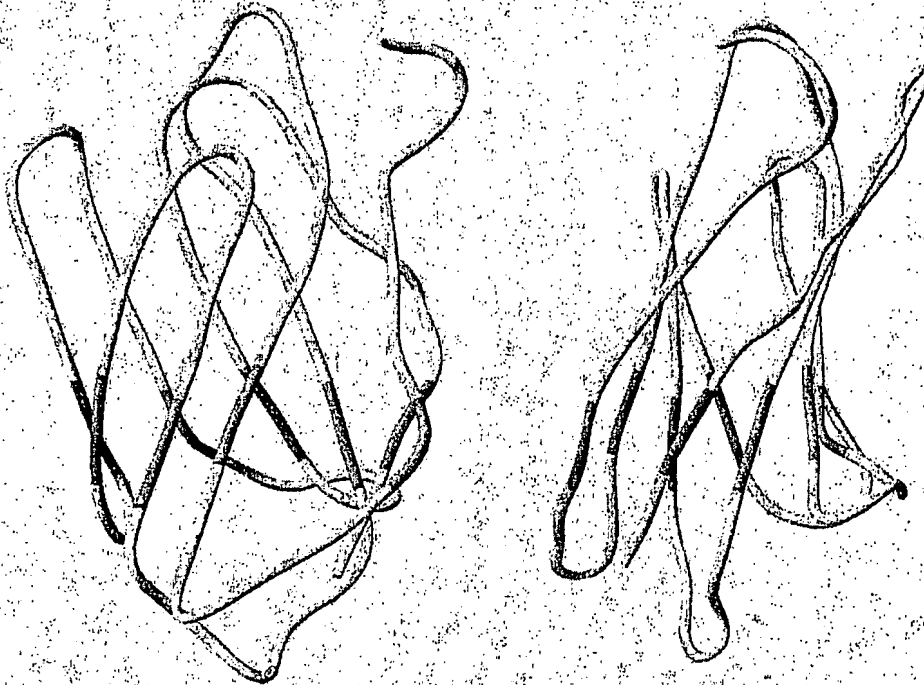
B



		A										B										C																				
hPD-1	1	P	P	T	F	F	P	A	L	L	V	V	T	E	G	D	N	A	T	F	T	C	S	F	S	N	T	S	E	S	F	V	L	N	W	Y	R	M	S	P	39	
hIgL-κ	1	Q	M	T	Q	S	P	S	S	L	S	A	S	V	G	D	R	V	T	F	T	C	R	S	S	Q	T	I	G	T	Y	L	N	W	Y	Q	Q	K	P	38		
hTCR α	1	Q	V	E	Q	S	P	P	D	L	I	L	Q	E	G	A	N	S	T	L	R	C	N	F	S	D	S	V	N	N	L	Q	W	F	H	Q	N	P	37			
hBTLA	1	Q	L	Y	I	K	R	Q	S	E	H	S	I	L	A	G	D	P	F	E	L	E	C	P	V	K	Y	C	A	N	R	P	H	V	T	W	C	K	38			
		C'										C''										D										E										
hPD-1	40	S	N	Q	T	D	K	L	A	A	F	P	E	D	R	S	Q	P	G	Q	D	C	R	F	R	V	T	Q	L	P	N	G	R	D	F	H	M	S	V	V	R	79
hIgL-κ	39	G	Q	A	P	K	L	L	I	F	A	A	S	S	L	L	N	G	V	P	S	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	S	75			
hTCR α	38	W	G	Q	L	I	N	L	F	Y	P	S	G	T	K	Q	N	G	R	L	S	A	T	T	V	A	T	E	R	Y	S	L	L	Y	I	S	S	74				
hBTLA	37	L	N	G	T	T	C	V	K	L	E	D	R	Q	T	S	W	K	E	E	K	N	I	S	F	F	I	L	H	F	E	P	67									
		F										G																														
hPD-1	80	A	R	R	N	D	S	G	T	Y	L	C	G	A	I	S	L	A	P	.	.	K	A	Q	I	K	E	S	L	R	A	E	L	R	110							
hIgL-κ	75	L	Q	P	E	D	F	A	T	Y	Y	C	Q	Q	S	H	S	A	P	.	.	P	Y	T	F	G	Q	G	T	R	L	E	M	K	105							
hTCR α	75	S	Q	T	T	D	S	G	V	Y	F	C	A	A	L	D	L	W	G	G	A	D	G	L	T	F	G	K	G	T	H	L	I	Q	106							
hBTLA	68	M	L	P	N	D	N	G	S	Y	R	C	S	A	N	F	Q	S	N	.	.	L	I	E	S	H	S	T	T	L	Y	V	T									

Figure 2

C

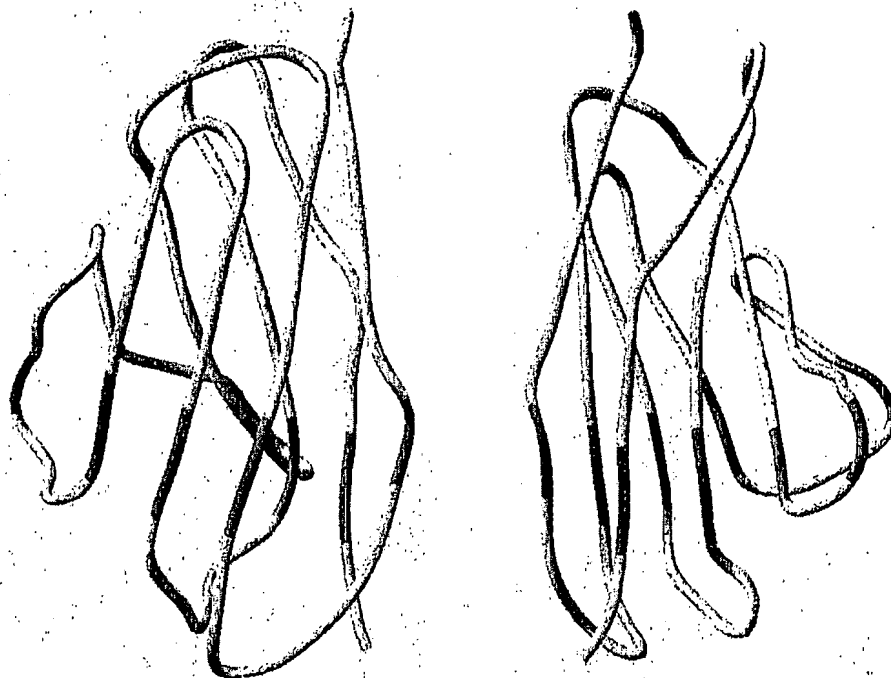


		A	A'	B	C	
hCD28	1	K I L V	K Q S P M L V A Y D N A V I N E S	C K Y S Y N L F I S R E F R A S L H K	38	
hCTLA-4	1	A M H V	A Q P A V V L A S S R G I A S F V	C E Y A S P G K A T E V R V T V L R	39	
hICOS	1	E I N G S	A N Y E M F F H N G G V	Q T L C K Y P D I V Q Q F K M Q L L K	37	
				*	*	
		C	C''	D	E	
hCD28	39	G L D S A V	E V C V V Y G N Y S Q Q L Q V Y S K T G F N C D G K L G N E S V T	77		
hCTLA-4	40	Q A D S Q V T E V C A A T Y M M G N E L T F L D D S	N C T G T S S G N Q V N	77		
hICOS	38	G G Q M L C D L T K T K G S G N T V S I K S L K E C H S Q L S N N S V S	73			
		*	*	*	*	
		E	F	G		
hCD28	78	F Y L Q N L Y V N Q T D I Y F C K T E V M Y P P P Y L D N E K S N G T I I H V	116			
hCTLA-4	78	L T I Q G L R A M D T G L Y T C K V E L M Y P P P Y Y L G I G N G T Q I Y V	115			
hICOS	74	F F L Y N L D H S H A N Y Y F C N L S I E D P P P F K V T L T G G Y L H T	110			
		*	*	*		



Figure 2

D



		A	B	C	
hPD-1	1	P P T F F P A L L V V T E G D N A T F T C S F S N T S E S F V L N W Y R M S P	39		
hlgL-κ	1	Q M T Q S P S S L S A S V G D R V T F T C R S S Q T I G T Y L N W Y Q Q K P	38		
hTCR α	1	Q V E Q S P P D L T L Q E G A N S T L R C N F S D S V N N L O W F H Q N P	37		
hBTLA	1	Q L Y I K R Q S E H S I L A G D P F E L E C P V K Y C A N R P H V T W C K	36		
		C'	D	E	
hPD-1	40	S N Q T D K L A A F P E D R S Q P G Q D C R F R V T Q L P N G R D F H M S V V R	79		
hlgL-κ	39	G Q A P K L L I F A A S S L L N G V P S R F S G S G S G T D F T L T I S S	75		
hTCR α	38	W G Q L I N L F Y P S G T K Q N G R L S A T T V A T E R Y S L L Y I S S	74		
hBTLA	37	L N G T T C V K L E D R Q T S W K E E K N I S F F I L H F E P	67		
		F	G		
hPD-1	80	A R R N D S G T Y L C G A I S L A P K A Q I K E S L R A E L R	110		
hlgL-κ	78	L Q P E D F A T Y Y C Q Q S H S A P P Y T F G Q G T R L E M K	106		
hTCR α	75	S Q T T D S G V Y F C A A L D L W G G A D G L T F G K G T H L I Q	105		
hBTLA	68	M L P N D N G S Y R C S A N F Q S N L I E S H S T T L Y V I T			